ANNUAL REPORT

OF

THE HOWE LABORATORY OF OPHTHALMOLOGY

HARVARD MEDICAL SCHOOL

1958

243 CHARLES STREET

BOSTON, MASSACHUSETTS

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Stanley Hersh, M.D.: *Research Fellow in Ophthalmology*

Kevin Hill, M.D.: *Research Fellow in Ophthalmology*

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IT was thirty years ago when the Howe Laboratory became an official department of Harvard Medical School and only slightly less than that when it became functionally operative at the Massachusetts Eye and Ear Infirmary. The Laboratory was a pioneer then and is a pioneer now, but with the privileges and responsibilities that go with maturity. What has been lacking in the way of financial security has been compensated for by the loyal support and understanding from its many friends inside and outside the medical profession. To all of these friends, our Annual Reports are dedicated.

Research Activities

Retinal studies. Like so many investigations in science, the studies on the retina to be noted here developed as a natural but unforeseen outgrowth of a study on a seemingly unrelated subject. Actually it was while studying fat processes in the cornea that Dr. Kuwabara observed the retina to be an unusually favorable site for the elucidation of some enzyme activities. Specifically it was found to be extraordinarily rich in a group of dehydrogenases that are concerned with energy production in tissue. The role of these enzymes in retinal metabolism is now being vigorously pursued and it is reasonable to expect information shortly which will have great significance for the normal retina and possibly for disease states involving the retina. One of the most interesting aspects that has already become evident is that Müller's fibers, which are modified glial cells and heretofore thought to have structural functions only, are in fact the richest source of some of these enzymes. It may well turn out that Müller's fibers comprise the power-pack of the retina. In these studies we have been most fortunate in having the close collaboration of Dr. Sidney Futterman of the Retrolental Fibroplasia Laboratory and the financial support of the Knights Templar Eye Foundation.

Ocular hydrodynamics and glaucoma. Through correlation of microdissection of the outflow channels (trabecular meshwork) with the facility of outflow of aqueous humor, it has been possible to ascertain the site of resistance for the normal flow of fluid out of the eye and, by inference, the site of abnormal resistance that is the cause of glaucoma. These researches, carried on systematically over the past several years by Dr. Grant under the auspices of the Alfred P. Sloan Foundation,

the Lovejoy Fund, and the Public Health Service, have yielded richly to contemporary knowledge of the subject.

It has been noted that physical forces can decrease the resistance to aqueous outflow in a manner similar to that induced by drugs employed in treating glaucoma and it has for the first time been demonstrated that the trabecular meshwork and the attached ciliary muscle are essential to this phenomenon. Now exploratory studies have been carried out to elucidate a related but opposite phenomenon in which an increase in resistance to outflow may be induced by physical distortion of tissues in the region of the trabecular meshwork. Experiments, as yet unpublished, suggest that forward displacement of the ciliary body will increase resistance to outflow irrespective of any role that the iris may play in obstruction. This is a new concept which may or may not turn out to have clinical applicability.

One of the main handicaps for glaucoma investigation has been the infrequency with which suitable glaucomatous eyes become available for research. One such eye of the so-called open-angle variety, did become available this past year and showed an increase in facility of outflow following trabeculotomy similar to that which has been found to occur with the normal eye.

Further studies connected with glaucoma have been: the analysis by Dr. Grant of the characteristics of a new electronic tonometer invented by Wilfred Roth; examination of a perilimbal suction cup designed by the Swedish investigators, Rosengren and Ericson, for experimental compression of the aqueous veins; evaluation of the distortion of outflow channels induced by fixatives employed in preparing eyes for histologic study and trial of new fixatives to minimize this distortion; and the use of an electronic analog computer for studies of the relationship between volume and pressure within the eye.

While the foregoing studies have centered about the outflow mechanism, Dr. Kupfer has been initiating studies on the inflow mechanism. By electrochemical means he is attempting to develop a method for continuously monitoring the production of aqueous humor in the unopened eye of rabbits.

Biochemistry. The biochemical studies of the lens have been pursued in the hope that they may contribute to an understanding of cataracts. The mechanisms by which the lens

derives biological energy which is necessary to maintain transparency have been the subject of many investigations in this Laboratory. The most recent approach to the understanding of the lens is the study of lens proteins. Joining Dr. Kinoshita's staff to aid in this study is Dr. Abraham Spector who was trained as a protein chemist at the New York University Medical School and at the Carlsberg Laboratories in Copenhagen. Dr. Spector is currently devising methods to isolate and study the various types of lenticular proteins. The organ culture method previously used for rabbit lens has now been adapted to study the synthesis and breakdown of proteins of the calf lens. By this method it is possible to incubate calf lenses for 24 hours without changes in transparency, hydration, or glutathione content and with a constant rate of utilization of glucose and production of lactic acid. The development of the lens culture technique, first developed in this Laboratory by Dr. Everett Kinsey, has made it possible to study the incorporation of amino acids into the lens proteins in an environment closely simulating the physiological conditions which exist in the eye.

In collaboration with Dr. Sidney Futterman of the Retrolental Fibroplasia Laboratory the striking aerobic glycolysis manifested by ocular tissues is being investigated by the biochemical group. The metabolism of glucose in the presence of oxygen by either the retina, cornea or lens results in the production of large amounts of lactic acid. This outstanding metabolic characteristic of ocular tissues is not generally observed in other mammalian tissues. The only exception is neoplastic tissue and here the metabolism appears similar to that of the ocular tissues. The explanation offered for this phenomenon has been that the aerobic metabolism of these tissues could not keep pace with the production of lactic acid from the glycolytic mechanisms. However, recent findings seem to suggest that the lactic acid dehydrogenase present in high concentrations in ocular tissue may play a role not previously suspected. This enzyme seems to function to some extent with the co-enzyme, triphosphopyridine nucleotide (TPN), whereas it was previously thought to react almost exclusively with diphosphopyridine nucleotide (DPN). Because of this property all mechanisms which yield reduced TPN may couple with lactic acid dehydrogenase resulting in the reduction of pyruvate to lactic acid in ocular tissue. These

findings may not only be important in understanding the metabolism of ocular tissues but may have an important bearing in the metabolism of those tissues, like neoplasms, which exhibit a marked aerobic glycolysis.

These biochemical studies are being supported by the Atomic Energy Commission and by the Institute of Neurological Diseases and Blindness of the Public Health Service.

Toxicology and the cornea. Research concerning the injurious effects of chemicals and drugs on the eye has been conducted by Drs. Grant and Kern in the Howe Laboratory for several years. Some of the information which has been accumulated from this research has direct clinical application; some has scientific value of another sort. The clinical program has centered about specific cases which have come to the Infirmary because of chemical burns of the eye. The related experimental program has been designed to provide fundamental knowledge of the way in which toxic substances damage the eye so as to be able to forestall the effects of new and unusual substances, and to improve therapeutic measures for the poisons commonly encountered.

As noted in previous Annual Reports, the toxic effect of certain metals on the cornea has been found to be due to a special tendency of these molecules to combine chemically with the tissue, particularly with the mucoprotein, and to cause physicochemical changes in the tissue. Moreover certain substances, particularly EDTA (ethylenediamine tetraacetate) had definite antidotal value. During the past year various organic bases have been similarly tested for this reactivity and toxicity but the results have not yet reached the stage for drawing conclusions.

The toxicologic studies on the cornea have led of necessity to an examination of the water and electrolytes normally present in the cornea and to investigation of the physiologic distribution and combination of these substances with the tissue. There has been no evidence found for the concept of "bound" water in the cornea such as is present in hide tissue. Moreover the common cations such as sodium, potassium, and calcium are found to be concentrated by the cornea to a greater degree than can be accounted for by the so-called Donnan effect. Even non-electrolytes such as sugars are found to be concentrated to some degree by the cornea. However, the

binding forces between physiologic or non-toxic substances and the cornea appear all to be much less than those involved in the binding of toxic substances.

An additional small investigation having some toxicologic implications has been concerned with the behavior of various gases injected into the anterior chamber of the eye. This study was prompted by the clinical problem of occasional damage to the cornea by adhesion of the vitreous humor to it following removal of a cataract. In treatment of this condition some advantage may be gained by keeping the vitreous away from the cornea by a bubble of gas to give the cornea time to heal. Air is customarily used for this purpose. However, it would presumably be advantageous to use a non-toxic gas which would remain for a longer time than air. In search of such a substance tests have been made of a series of gases in the anterior chambers of rabbits, employing only those gases expected to have little or no toxicity. Of those so-far tested (air, oxygen, carbon dioxide, argon, helium, sulfur hexafluoride, Freon-12, and butane) none, unfortunately, has been found to persist much longer than air. Air owes its persistence to its large nitrogen content, since oxygen alone disappears much faster. Carbon dioxide, as would be expected, goes very fast.

Fat formation. For the past several years, the subject of fat formation in the cornea and other tissues has occupied a conspicuous place in these Annual Reports. The entire subject, especially as it bears on atheroma and fatty degeneration, was presented in a semipopular form for a Lowell Lecture which will presumably be printed in book form along with other lectures of this series.

Several new observations have been consolidated during the past year. Thus, whereas oleic acid was previously found to be the sole precursor of sudanophilic fat, it has now been shown that palmitic and stearic acid form a birefringent lipid having the same distribution as the oleate-induced fat. Along with these histochemical studies, which have been carried out by Drs. Kuwabara and Cogan, correlative investigations of a more directly chemical nature have been made by Drs. Hill, Ciccarelli, and Kinoshita. It is now possible to state that the fats synthesized by corneal cells (and by many other tissues) consist for the most part of neutral glycerides.

While this process of fat formation by non-adipose tissue had been found to be an extraordinarily prompt process, occurring in a matter of hours, and eventually giving way to a more leisurely macrophage reaction, we had not, until this past year, appreciated its functional significance. It now appears that this energetic incorporation of fatty acids into neutral fats effectively removes the necrotizing and harmful fatty acids by binding them up into an innocuous and potentially useful form. That this process has not been recognized heretofore is probably attributable to the fact that it occurs in a pure form only early in the process of degeneration and that in later stages, when tissues are usually examined, it is masked by the macrophage reaction.

A curious biproduct of these studies has been the finding that the Purkinje fibers of the heart, comprising what is believed to be a conductive system, has a selective capacity for lipogenesis not shared by other portions of the cardiac muscle. This not only adds to the meager evidence showing metabolically distinct properties of the Purkinje system but has made possible for the first time a demonstration of the ramifications of Purkinje fibers in small animals (mice, rat, cat, and rabbit) analogous to what had previously been known to exist in larger animals.

The widespread implications of these fat studies, not so much for ophthalmology as for medicine in general, is of such seeming importance that further help has just been obtained in the person of Dr. John S. Andrews, a lipid chemist, and long-term support is being solicited to continue the work that has been conducted largely under the auspices of the American Heart Fund and the Greater Boston Chapter of the Massachusetts Heart Fund.

Neuro-ophthalmology. Histochemical studies, analogous to those noted last year on retinas of two patients with metachromatic leucoencephalopathy were repeated this year on the retinas of a patient with the Tay-Sachs form of amaurotic family idiocy. While these studies turned up little that was new or unanticipated they did provide documentation by modern histochemical means of the type and distribution of that glycolipid which accumulates in the retinas of patients with this particularly tragic inborn defect of metabolism.

In an attempt to correlate the retinal changes of this

disease with those in the brain, we were repeatedly side-tracked by the failure of previous reports in the literature to distinguish between various types of "amaurotic family idiocy." An article was therefore prepared suggesting that henceforth eponyms always accompany a report of amaurotic family idiocy to designate the type which is intended.

Interest in the clinical aspects of neuro-ophthalmology have been greatly intensified by Dr. J. Lawton Smith who is spending a year with us. Through his energetic and resourceful activities, we have had the opportunity of studying more fully the wealth of neuro-ophthalmic material at the Massachusetts General Hospital and the Massachusetts Eye and Ear Infirmary. This is being organized in the form of teaching conferences and in special studies of internuclear ophthalmoplegia, optico-kinetic responses in intracranial disease, and the ocular signs of carotid artery occlusion.

Photography. The production and cataloguing of stereophotographs illustrating ophthalmic disease has been a time-consuming and often costly function of the Howe Laboratory for almost ten years. The result has been, however, a documentary and teaching service that is unparalleled and well justifies the effort and money that has been put into it. Formal presentation of some of the collected material was made this past year by Dr. Donaldson at the several meetings of the New England Ophthalmological Society and at the International Congress of Ophthalmology. There has also been almost daily use of the material by the visiting staff, residents, medical students, and visitors. Approximately 750 slides, selected as being unusually good for teaching purposes, have been prepared with clinical summaries and discussions of each case for a sort of self-service instruction. Assisting in this preparation during the past year has been Dr. Stanley Hersh. Photomicrographic material has been added where available.

Additional sets illustrating neuroanatomic dissections have recently been made and the goniophotographic set has been revised and a third edition produced. These are available to other teaching institutions at cost. In addition, a new set consisting of 40 slides illustrating corneal degenerations and dystrophies is available at cost.

The great practical significance of the angle of the anterior chamber for glaucoma prompted the collection of the so-called

goniophotographs. In order to obtain better detail of the angle structures Dr. Donaldson has now made a special camera for goniophotography that permits double the previous magnification.

For the past five years much of the cost involved in developing these teaching aids has been borne by a training grant from the Public Health Service. This grant has now expired and applications are being made for continued development of the teaching collection on a project basis.

Miscellaneous projects. A study that was interesting, though of limited practical consequence, was made this past year on pingueculas. These peculiar tumors of the eye are often thought to be fat but in fact are composed of excessive amounts of tissue that stain like elastic tissue. To ophthalmic pathologists, therefore, they have been called hypertrophic elastic tissue. As a matter of fact, we have now shown that they do not dissolve on incubation with elastase and therefore are not true elastic tissue. Until a more definitive analysis of their structure is possible they should probably be called elastoid.

Further studies have been made on the objective testing of visual acuity in the newborn and early infantile period by Dr. John Gorman in collaboration with the Howe Laboratory. The opticokinetic test has been adapted for use in babies and approximately 100 normal infants have now been tested within the first four days after birth and a lesser number at several months of age. It appears that the acuity is equal to 20/200–20/400 soon after birth and this does not change for the first few months. It is hoped eventually to continue the study at still later months and to incorporate observations on cases with known defects in their visual system. Unfortunately the apparatus which has been developed for the newborn is not adequate for testing babies at six months of age or older.

A correlation of goniophotographs of the developing human eye and microscopic structures of the angle of the anterior chamber is being undertaken by Drs. Kupfer, Donaldson, and Ikui with the aim of applying the observations to congenital glaucoma. Presumably this disease is attributable to an arrested development of these structures and it is important to

have an understanding of the pathologic bases for the clinical signs.

The opportunity to examine the eyes of a large number of mongolian idiots enabled Dr. Donaldson to confirm and document the fact that they have characteristic iris markings. This abnormality, consisting of white areas, called Brushfield spots, at the iris roots, may contribute importantly to the early recognition of mongolian idiocy.

Many more investigations are in the pilot stage or under contemplation awaiting means of support, space, or proper personnel. Some of those which have at least reached the discussional stage are diabetic retinopathy, retinitis pigmentosa, and epithelial wound healing.

Service Activities

Service functions are now taken for granted and may be passed over with little more than mention. The well-nigh unique situation of the Howe Laboratory as a functional part of a hospital with a distinct administrative set-up has enabled the Laboratory, unencumbered by routine obligations, to provide facilities which are rarely, if at all, available elsewhere. Thus we have what is probably the most complete collection of photographs of clinical cases anywhere available. We have the close cooperation of a routine pathology laboratory with an experimental pathology laboratory. We have a consultation service that, in accessibility and possibly in authority, is rarely paralleled elsewhere. This is particularly active at present in the fields of neuro-ophthalmology and glaucoma. We have a reservoir of teachers that represent most of the basic sciences in ophthalmology and an excellent ophthalmic library. Most particularly we have a friendly and stimulating association with the staffs of the Massachusetts Eye and Ear Infirmary and other institutions.

Organization and Support of the Laboratory

When plans were being drawn up some seven years ago, for what is now the physical plant of the Howe Laboratory, 4500 square feet seemed well nigh ideal. At that time we did not

envisage the extent to which the government would give fellowship and project support to studies and investigators. Nor did we, accustomed as most investigators are to improvisation, realize the magnitude of support which might come from various individuals and beneficent agencies. Only when the blueprints were in an irreversible stage did it become apparent that the space of 4500 square feet (almost double that of the former space) would still be quite inadequate. It has, therefore, been a continuing hope that we might obtain additional quarters. Some time ago a vacant spot on the roof was tentatively selected as a possible site for the construction of an annex that would give us 2,000 square feet. Now, thanks to the intercession of Dr. Dunphy and the generosity of the Massachusetts Lions Clubs, it is possible to announce that money has been promised, matched by other funds mostly from the Federal Government, to construct such an annex. Tentatively it is planned to make the space available to at least one career investigator and to accommodate young investigators temporarily attached to the Laboratory.

The perennially awesome problem of balancing the budget was again ameliorated this year by donations from a group of benevolent individuals, whom it is a pleasure to list in this Report, and by generous gifts from the Knights Templar Eye Foundation and, as this Report goes to press, by the Max, Martha, and Alfred M. Stern Fund. Only a person who has had to fit resources into the unpredictable demands of research can appreciate how indispensable unrestricted money is.

Our immediate situation is sound and we have confidence in the future but added endowment will have to be obtained for tenure appointments. It is fair to encourage bright young men to make a career of ophthalmic research only if there is reasonable assurance of maintaining some at least on a tenure basis. The number of tenure appointments at the Howe Laboratory, presently limited to two, should be increased. Accordingly efforts are being made to obtain funds in endowment size.

It is with deep appreciation that I record the following who have greatly helped in the support of the Laboratory this past year:

For general expenses:

Massachusetts Eye and Ear Infirmary
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DAVID G. COGAN, M.D.
Director

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LECTURES

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The ocular fundus. Postgraduate Course in Cardiology, Massachusetts General Hospital, in Boston, Massachusetts, March 4, 1958.

Corneal degeneration. Cincinnati Ophthalmological Society, in Cincinnati, Ohio, March 12, 1958.

Optic neuritis. Ophthalmic Pathology Club, in Washington, D. C., March 25, 1958.

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Diplopia. Panel discussion. Boston City Hospital, Eye, Ear, Nose and Throat Alumni Association, in Boston, Massachusetts, April 30, 1958.

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Ocular effects of radiation. Section on Industrial Medicine, Massachusetts Medical Society, in Boston, Massachusetts, May 21, 1958.

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Demonstration of ocular effects of diabetes. New England Ophthalmological Society, in Boston, Massachusetts, November 19, 1958.

COGAN, D. G. (*continued*)

Ophthalmic pathology. Harvard Medical School, Department of Pathology, in Boston, Massachusetts, December 13, 1958.

House Officer Lectures, Massachusetts Eye and Ear Infirmary
Effects of radiation on the eye. April 3, 1958.
Analysis of funduscopic photos of vascular disease. September 25, 1958.
Degenerative disease of the cornea, I. September 30, 1958.
Degenerative disease of the cornea, II. October 7, 1958.

DONALDSON, D. D.

Unusual conditions of the anterior segment of the eye. Connecticut State Medical Society, in Straford, Connecticut, May 1, 1958.

Diseases involving the chamber and angle. Brooklyn and Long Island Chapter of the American College of Surgeons, in Boston, Massachusetts, May 24, 1958.

Eye manifestations of systemic diseases. Veterans Administration, in Boston, Massachusetts, June 3, 1958.

New England Ophthalmological Society
Diseases and inflammatory conditions of the cornea. January 15, 1958.
Tumors and cysts of iris and ciliary body. February 19, 1958.
The diseases involving the chamber and angle. March 19, 1958.
Developmental and hereditary anomalies of the eye. April 16, 1958.
Exophthalmos and lesions of the orbit. December 18, 1958.

House Officer Lectures, Massachusetts Eye and Ear Infirmary
Eye manifestations of systemic diseases. June 3, 1958.
Traumatic lesions. December 11, 1958.

GRANT, W. M.

Tonography. Josiah Macy Jr. Foundation Conference Program, Third Symposium on Glaucoma, in Princeton, New Jersey, January 8–10, 1958.

with Chandler, P. A. Problems in glaucoma. New England Ophthalmological Society, in Boston, Massachusetts, January 15, 1958.

Research aspects of glaucoma. New York Academy of Medicine, Section on Ophthalmology, in New York, New York, February 17, 1958.

Postgraduate Assembly of the Oregon Academy of Ophthalmology and Otolaryngology, in Portland, Oregon.
Glaucoma, Part I and Part II, March 24, 1958.
Glaucoma, Part III, March 25, 1958.

Studies on the trabecular meshwork. Annual Meeting of the Massachusetts Eye and Ear Infirmary Alumni Association, in Boston, Massachusetts, April 15, 1958.

Postgraduate Glaucoma Course, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, May 2, 1958.

Pathology of glaucoma.

Research in glaucoma.

Toxicology, tonometry and tonography. Series of lectures to the Lancaster Courses in Ophthalmology, in Waterville, Maine. August 4–5, 1958.

Ophthalmic pharmacology. Harvard Medical School, Department of Pharmacology, in Boston, Massachusetts, September 16, 23 and 30, 1958.

Toxicology. Lecture to Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, October 17, 1958.

Congenital glaucoma. House Officer Lecture, Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, October 30, 1958.

KERN, H. L.

Interaction of acidic and basic dyes with beef corneal stroma. Third Ophthalmic Biochemistry Conference, in Cambridge, Massachusetts, February 24, 1958.

Biochemistry of the cornea. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 24, 30 and October 7, 1958.

KINOSHITA, J. H.

Eastern Section Meeting of the Association for Research in Ophthalmology, in Bethesda, Maryland, January 18, 1958.

The effect of glutathione on the formaldehyde oxidation in the retina.

with Merola, L. O. The distribution of glutathione and protein sulfhydryl groups in calf and cattle lenses.

Metabolism of glucose and pyruvate in the lens. Third Ophthalmic Biochemistry Conference, in Cambridge, Massachusetts, February 24, 1958.

Some unusual aspects of lens metabolism. Alumni Association Meeting of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 15, 1958.

Biochemical approaches in the study of cataracts. Research Committee of the Massachusetts Eye and Ear Infirmary, in Boston, Massachusetts, April 30, 1958.

Discussion: "Lens Potential," M. A. Constant. Twenty-seventh Annual Meeting of the Association for Research in Ophthalmology, in San Francisco, California, June 24, 1958.

The effect of age on the carbohydrate metabolism of bovine lens. Symposium on Cataracts. Eighteenth International Congress of Ophthalmology, in Brussels, Belgium, September 11, 1958.

The possible significance of the hexose monophosphate shunt pathway in lens. Conference on Lens. University of Strasbourg, in Strasbourg, France, September 15, 1958.

Discussion of the biochemical studies of the lens. Nuffield School of Ophthalmology, University of Oxford, in Oxford, England, September 17, 1958.

Biochemistry of the lens and cornea. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in oBston, Massachusetts, September 24–October 10, 1958.

Eastern Section Meeting of the Association for Research in Ophthalmology in New York, New York, November 22, 1958.

with Merola, L. O. The reactivity of the sulfhydryl groups in bovine lens.

with Futterman, S. Studies of the mitochondria of the retina. The effect of pontocaine on the carbohydrate metabolism of corneal epithelium.

KUWABARA, T.

with Cogan, D. G. (see Cogan, D. G.)

Retinal histochemistry. Series of lectures to the Postgraduate Course in Ophthalmology, Harvard Medical School, in Boston, Massachusetts, September 24–October 10, 1958.

with Cogan, D. G. Histochemical studies of retinal dehydrogenases. Eastern Section Meeting of the Association for Research in Ophthalmology, in New York, New York, November 22, 1958.

LEE, P.-F.

New England Ophthalmological Society Meetings, in Boston, Massachusetts.

with Henry, M. Clinical comparison of dichlorphenamide with diamox. February 19, 1958.

The influence of systemic steroid therapy on the intraocular pressure. March 19, 1958.

Gonioscopy. April 16, 1958.

Peripheral iridectomy on angle-closure glaucoma. Follow-up studies. December 17, 1958.

MEROLA, L. O.

with Kinoshita, J. H. (see Kinoshita, J. H.)

SMITH, J. L.

Neuro-ophthalmology. Connecticut Postgraduate Seminar in Psychiatry and Neurology, in New Haven, Connecticut, October 20, 1958.

Neuro-ophthalmology. Veterans Administration, in Boston, Massachusetts, November 14, 1958.

SNYDER, C.

Abe's illusion. New England Ophthalmological Society, in Boston, Massachusetts, February 19, 1958.

Presentation of an instrument. New England Ophthalmological Society, in Boston, Massachusetts, March 19, 1958.

What mother saw. New England Ophthalmological Society, in Boston, Massachusetts, April 16, 1958.

EXHIBITS

DONALDSON, D. D.

Corneal Dystrophy Exhibit. International Congress of Ophthalmology, in Brussels, Belgium, September 6–13, 1958.

Corneal Dystrophy Exhibit. New England Ophthalmological Society, in Boston, Massachusetts, November 19, 1958.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I Give and Bequeath to the Howe Laboratory of Ophthalmology .....Dollars to be Applied to the Uses of Said Laboratory.

Such bequests are managed by the Treasurer's Office of Harvard University, and the income is accredited to the Laboratory.